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Antitachycardia Devices: Realities and Promises

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Nonpharmacologic therapy for ventricular arrhythmias has gained growing attention with the development of the implantable cardioverter-defibrillator. In addition, the reports of adverse effects of drug therapy from several studies, including the Cardiac Arrhythmia Suppression Trial (CAST), have supported the need for these devices. The development of new implantable cardioverter-defibrillators that have the capability of antitachycardia pacing, bradycardia pacing, cardioversion and defibrillation has enhanced their clinical utility.

The currently available implantable cardioverter-defibrillators have been shown to significantly improve survival after sudden cardiac arrest in patients with life-threatening ventricular arrhythmias. Newer devices with expanded capabilities may reduce mortality even further. In this report the features of currently available antitachycardia devices and implantable cardioverter-defibrillators are reviewed and the features and current implant data on newer antitachycardia devices are discussed.

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Management of patients with hemodynamically important arrhythmias has become an increasingly complex problem for cardiologists because of the ever growing available treatments for both supraventricular and ventricular tachyarrhythmias. Important therapeutic decisions include not only when to treat and how to judge efficacy of treatment (1), but also how to choose from among the many therapies available, including pharmacologic agents, catheter ablation, arrhythmia surgery and antitachycardia device implantation.

Antiarrhythmic Therapy

The growth and development of antitachycardia devices have been accelerated by inefficacy or side effects, or both, inherent in drug management. Pharmacologic therapy has always been the mainstay of treatment for both supraventricular and ventricular arrhythmias. Although antiarrhythmic medications continue to be the primary therapy used by most cardiologists treating arrhythmias, an agent capable of preventing arrhythmia inducibility by programmed stimulation is found in only 10% to 30% of patients with life-threatening ventricular arrhythmias, although the percentage is somewhat higher for patients with supraventricular arrhythmias. Further, side effects from antiarrhythmic medications may prompt discontinuation of, or poor compliance with, therapy by many patients, leading to drug inefficacy. Many patients, especially those with supraventricular arrhythmias, are young and do not find appealing the prospect of taking antiarrhythmic medications for many years, particularly during childbearing periods. Other problems with antiarrhythmic medications include arrhythmia aggravation, as emphasized by the recent CAST trial (2). Some investigators (3–6) have recommended wider use of amiodarone either with or without guidance from electrophysiologic testing, but the risk of side effects (5% to 7% pulmonary toxicity risk alone) (7) and significant recurrence rate of ventricular tachycardia (10% to 30% at 2 years) (8) has limited the usefulness of this drug.

Catheter ablation has shown promise for both ventricular (9) and supraventricular (10,11) arrhythmias. Ablation has been highly successful for patients with the Wolff-Parkinson-White syndrome and atrioventricular (AV) node reentry. It has also been effective in creating heart block as a therapeutic approach in patients with intractable atrial arrhythmias or atrial flutter-fibrillation in whom pharmacologic therapy has been unsuccessful. Catheter ablation for ventricular tachycardia appears to be most useful in "idiopathic" ventricular tachycardia (12,13) but some success has been reported (14–16) in more common types of this arrhythmia.

Surgery for ventricular tachycardia has been highly successful and is now accepted as standard therapy for many patients. This approach is limited by the relatively small subset of patients (10% to 15%) who are appropriate candidates, the significant operative mortality rate (9% to 15%) (17–20) and the surgical and mapping expertise required by the physicians performing the procedure.

Thus, the impetus for the development of antitachycardia

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devices has been strong even though they are in a sense an admission of failure to find a curative or suppressive therapy. Nonetheless, their efficacy and acceptance by patients have been excellent and technologic advances in the field are occurring rapidly. This review will focus on the current status of antitachycardia devices, including those that are currently in the investigational stage of development.

Antitachycardia Pacing

Tachycardia Prevention

Overdrive atrial or ventricular pacing to suppress ventricular arrhythmias has been tried, but the long-term success for tachycardia suppression is poor in patients with a normal heart rate (21,22). Overdrive pacing has been used successfully to prevent tachycardias that emerge from sinus bradycardias or AV block or in patients with the long QT syndrome (23,24). Dual-chamber pacing with a short AV interval has prevented some supraventricular arrhythmias, particularly AV node reentry (25). Although this approach may be helpful, the hemodynamic problems associated with this technique (and curative therapy now available) make it clinically unappealing (25).

Other pacing techniques to prevent tachycardia onset have been tried. For example, premature subthreshold stimulation during the effective refractory period (Fig. 1) can inhibit the next stimulated complex and terminate some tachycardias by prolonging local refractoriness (26,27). Subthreshold stimulation has not been clinically useful in preventing the initiation of tachycardia or in terminating tachycardias reliably (28). High current strength pacing at the site of origin of tachycardia prevented induction of ventricular tachycardia in nearly 50% of patients in one study (29). Although the mechanism of this observation is unclear, the frequent finding of multiple ventricular tachycardia configurations in an individual patient and the difficulty in maintaining an electrode at the site of origin of ventricular tachycardia in the left ventricle limits the clinical utility of this technique.

Tachycardia "annihilation" with use of critically timed and positioned subthreshold or hyperpolarizing stimuli has been described, but has found little clinical use except for parasystolic rhythms (30). Thus, despite the need for tachycardia prevention, clinically important and desirable techniques to achieve it have been frustratingly inadequate.

Detection of Tachycardia

Automatic tachycardia detection algorithms. Early generations of antitachycardia devices were patient activated and depended on the accurate interpretation by the patient on the basis of symptoms that the tachycardia had started. More recent generations of devices have had automatic tachycardia detection algorithms. Although reliance on rate as the only detection criterion has a high sensitivity, specificity is low; therefore, other rhythms, either physiologic (sinus tachycardia, for example) or pathologic (atrial fibrillation), can trigger device discharge and lead to inappropriate therapy. Therefore, other criteria to improve the specificity of tachycardia recognition have been incorporated into some devices but with only mixed success. For example, measuring differences in timing and sequence between two ventricular electrodes as a means of differentiating premature ventricular complexes from sinus beats showed that 14 of 15 ventricular ectopic configurations exhibited a >40 ms difference in timing compared with sinus beats (31). If the ventricular tachycardia exhibits ventriculoatrial conduction, a single premature (80 to 100 ms) atrial extrastimulus can be used to exclude sinus tachycardia by failing to produce a significant change in ventricular cycle length (32). Electrogram analysis can be used to discriminate anterograde and retrograde atrial depolarization on the basis of amplitude and slew rate differences (33). Analysis of simultaneous atrial and ventricular recordings to identify AV dissociation (34) and recording right ventricular pressure (35) can help differentiate ventricular tachycardia from sinus tachycardia.

Other arrhythmia detection criteria. It is quite clear that no detection algorithm is perfect and the ideal system may need to employ several algorithms, including biosensors. Still, overlapping features of different tachycardias will continue to occur, necessitating individualization of therapy by carefully programming the device for each patient. Other arrhythmia detection criteria, such as suddenness of tachycardia onset, rate stability and maintenance of a high rate, have improved tachycardia detection algorithms but have not been as useful clinically as it was initially hoped (36).

Tachycardia Termination

Mechanism of termination. Many, perhaps most, tachyarrhythmias that occur clinically are due to reentry. Penetration into the reentrant circuit by a paced complex depends on the presence of excitable tissue between the leading edge and "tail" of the electrical wave front propagating in the circuit (often referred to as the "excitable gap"). A paced impulse can reset the tachycardia circuit when it collides with the leading edge of the depolarizing wave front but propagates anterogradely in nonrefractory tissue. It then advances the tachycardia circuit (37–40). When this phenomenon occurs with continuous pacing, the arrhythmia is said to be "entrained" (41). At shorter extrastimulus intervals, the impulse can collide with the propagating wave front both anterogradely and retrogradely and terminate the arrhythmia. The relative refractoriness of the tissue within the "excitable gap," as determined by the resetting response of tachycardia to an extrastimulus, is a major determinant of the ability of the paced extrastimulus to terminate sustained monomorphic ventricular tachycardia (36,39).

Termination algorithms. The ability to enter the excitable gap of a tachycardia circuit depends on the site and timing of stimulation and the number and energy of the extrastimuli (42). Many algorithms for arrhythmia termination have been

investigated. However, an algorithm that is effective in the electrophysiology laboratory may not be effective once the patient is ambulatory. Autonomic discharge in response to postural changes may alter conduction times and refractory periods for both ventricular and supraventricular arrhythmias (43). Pacing modes using pacing bursts or extrastimuli introduced as a percent of the sensed tachycardia rate (adaptive modes) are probably superior to modes using fixed or predetermined coupling intervals (44). Further, in view of the potential risk of accelerating ventricular tachycardia to a hemodynamically unstable arrhythmia in up to 36% of patients (45), backup defibrillation is mandatory when attempting pacing termination of ventricular tachyarrhythmias. A pacing mode using automatically increasing numbers of stimuli with adaptive coupling intervals ("universal antitachycardia mode") has been shown to be effective and is being incorporated into some investigational antitachycardia devices (46,47). This method of pacing is more effective than single-, double- or overdrive burst pacing and terminated 92% of induced ventricular tachycardia episodes compared with 56% for overdrive burst pacing in the same patients (47). Such adaptive modes reduce the importance of spontaneous variations in tachycardia cycle length or changes in tachycardia rate induced by pacing.

Some newer techniques that are still investigational include delivery of ultra rapid trains of stimuli with frequencies up to 100 Hz to obtain a single ventricular capture at the end of ventricular refractoriness. However, this approach achieves a success rate of only 50% to 60% for termination of tachycardia (48). As discussed previously, other investigators have used subthreshold stimulation ("inhibition") to prevent premature ventricular extrastimuli in dogs (26) and humans (27) (Fig. 1). This technique has also been used to terminate both supraventricular (49) and ventricular (50) tachycardia. Although promising, subthreshold stimulation is limited by the requirement of pacing close to the site of the reentrant circuit, which may be difficult to find or may involve multiple sites.

Clinical Efficacy of Antitachycardia Pacing

There are few large studies on efficacy of antitachycardia pacing. One report (51) of 53 patients who received an antitachycardia pacemaker for supraventricular and ventricular arrhythmias reviewed a 14-year experience with these devices. Among patients with an antitachycardia pacemaker for supraventricular tachycardia who were followed up for a mean of 68 months, 93% had successful termination of tachycardia by pacing at 1 year and 78% at 5 years. In 20 patients with an antitachycardia pacemaker for termination of ventricular tachycardia followed up for a mean of 37 months, efficacy was stated to be 78% at 1 year and 55% at 5 years. The occurrence of sudden death in 4 of these 20 patients was not believed to be related to the pacemaker.

In a multicenter study (52) 63 patients had an antitachycardia pacemaker implanted for supraventricular arrhythmias and were followed up for 30 months. Of these patients, 45% had arrhythmia control with pacemaker therapy alone, 49% required concurrent drug therapy for control of recurrent arrhythmias, 6% were nonresponders and 6% required explantation of the pulse generator for a variety of reasons. A third study (53) demonstrated an improvement in employability and quality of life in patients who received an automatic antitachycardia pacemaker for supraventricular tachycardia. In the period of testing noted earlier, lack of backup defibrillation in antitachycardia pacemakers precluded their use in patients with ventricular tachyarrhythmias. Now that such backup is available, indications for implanting these devices will expand and larger clinical studies will clarify the role of antitachycardia pacing in patients with ventricular tachycardia.

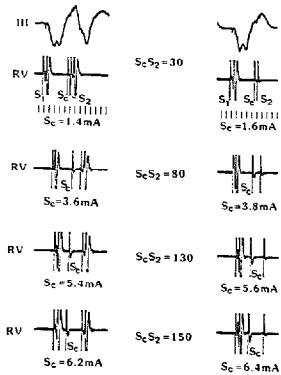

Figure 1. Inhibition of a ventricular premature beat in the human ventricle by a subthreshold "conditioning" (S_c) stimulus. The S_1S_2 interval was 270 ms. On the **left**, for each S_cS_2 the highest S_c (mA) at which no inhibition occurs is shown. On the **right**, the lowest S_c (mA) at which S_2 was inhibited is depicted. As the S_cS_2 interval increases, the current of S_c needed to inhibit S_2 increases. Time intervals are 50 ms. RV = right ventricle. Reprinted from Prystowsky et al. (27) with permission from the American Heart Association, Inc.

Limitations of Antitachycardia Pacemakers

Risk of ventricular fibrillation. The most important limitation of antitachycardia pacing for patients with ventricular tachycardia is the risk that the arrhythmia will accelerate to ventricular fibrillation. This event occurs in more than one third of patients when pacing is used during electrophysiologic studies to terminate ventricular tachycardia (54). Availability of backup defibrillation in the same device eliminates

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sudden cardiac death from this change in rhythm but does not prevent syncope. In patients with an antitachycardia pacemaker for supraventricular tachyarrhythmias, recognition of coexistent arrhythmias not amenable to antitachycardia pacing, such as atrial fibrillation, can be a difficult problem.

Induction of atrial fibrillation or flutter during pacing to terminate supraventricular tachycardias. This has been noted in up to 8% of trials and in 30% of patients (55). Pacing-induced atrial fibrillation was *sustained* in 75% of the patients in these trials (55), an event that is potentially catastrophic in patients with the Wolff-Parkinson-White syndrome, who may be subject to rapid anterograde conduction over an accessory pathway (56).

Summary

Antitachycardia pacemakers have a limited clinical role as the sole therapy for supraventricular arrhythmias particularly because catheter ablation techniques can eliminate most of the tachycardias to be treated. Occasionally, in a patient who also has symptomatic bradyarrhythmias that require pacing, antitachycardia pacing for supraventricular tachycardia may be indicated. Antitachycardia pacemakers without backup defibrillation are contraindicated for patients with ventricular tachycardia. Devices with combined antitachycardia pacing, bradycardia pacing and defibrillation are currently under investigation and are described below.

Cardioversion and Defibrillation

Mechanism

Cardioversion. Most episodes of sustained ventricular tachycardia are probably due to reentry, although this origin is difficult to prove definitively. Successful cardioversion of ventricular tachycardia is thought to be due to depolarization of tissue (either partially or fully recovered and therefore excitable) in the reentrant circuit. Low energy shocks (≤0.05 J) were shown by Saksena et al. (57) to capture excitable myocardium locally and then spread to the origin of ventricular tachycardia. Higher energy shocks (>0.5 J) captured sites in the ventricle both at the site of origin of ventricular tachycardia and at distant sites. Cardioversion of ventricular tachycardia, particularly with low energy shocks, must be synchronized to the QRS complex to avoid activating myocardium during the vulnerable period (early to midportion of the T wave on the scalar electrocardiogram [ECG]) when recovery of myocardial excitability is not uniform and induction of ventricular fibrillation or reinduction of ventricular tachycardia is more likely (58).

Defibrillation. The mechanism of defibrillation is probably different from that of electrical cardioversion for ventricular tachycardia. Zipes et al. (59) showed that a critical mass of ventricular myocardium must be depolarized during defibrillation to terminate ventricular fibrillation. The size of this critical mass is often <100% of the ventricular myocardium (60). Others (61) have demonstrated the need to achieve a critical threshold energy (in dogs) for successful defibrillation. Lower energy levels caused local defibrillation, but also reinitiation of ventricular fibrillation in other tissues, leading to failure of the shock to terminate ventricular fibrillation.

Low Energy Cardioversion

Several investigators (62–66) have demonstrated the feasibility of low energy synchronous cardioversion of ventricular tachycardia with use of a catheter electrode. After these initial studies, an implantable catheter cardioverting system was implanted in seven highly selected patients with slow, hemodynamically tolerated ventricular tachycardia (67). In that study all episodes of ventricular tachycardia had to be reliably terminated with ≤1.7 J on at least three separate occasions without evidence of acceleration of the arrhythmia. One of these seven patients was discharged from the hospital with the device in an automatic mode and had recurrence of ventricular tachycardia. The cardioverter discharge terminated the tachycardia but caused atrial fibrillation that led to prompt hospitalization. The new arrhythmia led to a ventricular rate response above the rate threshold and resulted in several automatically delivered shocks; one of these produced ventricular fibrillation from which the patient was promptly resuscitated. This study demonstrated both the feasibility of low energy cardioversion and the need for backup defibrillation.

As of 1987, 31 cardioverters (Medtronic model 7210) had been implanted (68). Because of the limited applicability of the device, the concept of the implantable cardioverter was subsequently incorporated into devices also capable of backup defibrillation. The efficacy of low energy cardioversion in terminating ventricular tachycardia is equal to that of antitachycardia pacing (69,70). However, arrhythmia acceleration rates were higher with cardioversion and shocks were less well tolerated than with pacing. Also, low energy cardioversion resulted in a 23% incidence of atrial arrhythmias, a phenomenon not seen with antitachycardia pacing (69).

Implantable Cardioverter-Defibrillators

Indications. The North American Society of Pacing and Electrophysiology has provided a set of indications for implantation of a cardioverter/defibrillator (71). Three classes of indications have been suggested: *class I*, the consensus is that implantable cardioverter-defibrillator therapy is indicated; *class II*, such therapy is an option, but a consensus does not exist; and *class III*, such therapy is generally not justified. The following were suggested as *class I* indications: 1) one or more episodes of spontaneous sustained ventricular tachycardia or ventricular fibrillation in a patient in whom electrophysiologic testing or spontaneous ventricular arrhythmias, or both, could not be used accu-

rately to predict efficacy of the therapies; 2) recurrent episodes of spontaneous sustained ventricular tachycardia or ventricular fibrillation despite antiarrhythmic drug therapy (guided by electrophysiologic testing or noninvasive methods); 3) spontaneous sustained ventricular tachycardia or ventricular fibrillation when antiarrhythmic drug therapy is limited by intolerance or noncompliance; and 4) persistent inducibility of clinically relevant sustained ventricular tachycardia or ventricular fibrillation at electrophysiologic study during administration of the best available drug therapy or despite surgical or catheter ablation in a patient with spontaneous sustained ventricular tachycardia or ventricular fibrillation.

These four class I indications for implantable cardioverter-defibrillator therapy can be reduced to the following: the patient has ventricular tachycardia or ventricular fibrillation for which no other therapy is successful by virtue of drug inefficacy or patient intolerance or noncompliance; surgical or ablation therapy is contraindicated; or no satisfactory end point exists to judge therapeutic efficacy.

Class II indications include syncope of undetermined origin in a patient with clinically relevant sustained ventricular tachycardia or ventricular fibrillation induced at electrophysiologic study in whom antiarrhythmic drug therapy is limited by drug inefficacy or patient intolerance or noncompliance.

Class III indications include 1) sustained ventricular tachycardia or ventricular fibrillation that is mediated by acute ischemia or infarction or of a toxic or metabolic origin and amenable to correction or reversibility; 2) recurrent syncope of undetermined origin in a patient without inducible sustained ventricular tachyarrhythmias; 3) incessant ventricular tachyarrhythmias; 4) ventricular fibrillation secondary to atrial fibrillation in the Wolff-Parkinson-White syndrome in a patient whose bypass tract is amenable to surgical or catheter ablation; and 5) surgical, medical or psychiatric contraindications.

Specifications and functions. Currently only the AICD (Cardiac Pacemakers) is approved by the Food and Drug Administration in the United States, although other devices are currently under investigation and several should be approved soon. More than 7,000 nonprogrammable AICDs have been implanted worldwide. The current generation of the device (model 1550) weighs 235 g, displaces 145 cc and is powered by two lithium-silver vanadium pentoxide cells. The pulse generator delivers truncated exponential shocks of 26 or 30 J synchronized to the detected QRS complex by a sensing circuit. The device is capable of delivering up to 200 shocks over its life span, which averages 24 to 36 months.

Bipolar sensing of the ventricular electrogram determines the detected heart rate and acts to synchronize delivery of the cardioverting shock, usually over two silicone-insulated epicardial or pericardial patch leads positioned on the right and left ventricles (72). In addition, the AICD offers the probability density function, which is an analysis of the proportion of the cardiac cycle that the ventricular electrogram spends on the isoelectric line. Theoretically, the probability density function should distinguish ventricular fibrillation and wide QRS tachycardias, such as ventricular tachycardia, that spend only a small portion of the cardiac cycle at the isoelectric line from narrow QRS supraventricular tachycardias that occupy the isoelectric line for a greater proportion of the cardiac cycle. In fact, however, the clinical utility of the probability density function is marginal and may prevent the appropriate detection of ventricular tachycardia with a relatively narrow QRS complex and may increase the time required for arrhythmia detection (73). The model 1550 has a programmable tachycardia detection rate and the probability density function can be activated or deactivated.

With this currently available device, when the rate counter has recorded eight beats that fulfill the rate-detection criterion, a charging cycle is started after a delay of 2.5 s to assure that the arrhythmia is sustained. Including the time required for arrhythmia recognition (<5 s), a 2.5 s delay and charging time (usually 6 to 7 s), the total duration of an arrhythmia before delivery of a defibrillation shock is usually <25 s. The device is "committed," meaning that once an arrhythmia has been detected and the capacitors have been charged, a shock will be delivered whether or not the arrhythmia has spontaneously terminated. If the arrhythmia is not terminated with the first shock, a second detection interval begins and the capacitors are recharged. As many as five shocks can be delivered for a single arrhythmic event. An interval of at least 35 s of a cardiac rhythm that does not satisfy the detection criteria (that is, return of sinus rhythm) must elapse before the device resets and is capable of delivering other defibrillation shocks.

Efficacy. The rate of sudden cardiac death after implantation of the AICD has averaged 2%/year (74–77). This rate compares favorably with that of historical control patients who have survived sudden cardiac death and who have a recurrence rate of 20% to 30% at 1 to 2 years of follow-up (78,79). When one combines sudden death and "appropriate" shocks to arrive at a "total sudden death incidence," an actuarial survival rate free of sudden cardiac death (sudden deaths and aborted sudden deaths) of 56% at 1 year and 14% at 4 years for patients with an AICD has been reported (80). Overall, among all patients with an implantable defibrillator, the incidence of at least one AICD discharge for a presumed sustained ventricular arrhythmia (that is, an "appropriate" shock) is 34% (81). It is more difficult to show an impact on overall survival. One recent multicenter study (82) of 955 patients reported a 62.5% survival rate at 6 years of follow-up. Patients who develop ventricular tachycardia or ventricular fibrillation also usually have left ventricular dysfunction due to either coronary disease or cardiomyopathy. Thus, although ventricular tachycardia and ventricular fibrillation may be well managed by the implantable defibrillator, congestive heart failure, recurrent myocardial infarction and occasionally pulmonary embolism remain important causes of death in many of these patients. Because of the unan-

swered questions about overall survival data, several controlled, randomized studies have been established, comparing implantation of a cardioverter-defibrillator with other forms of treatment.

Limitations and complications. The perioperative mortality associated with cardioverter-defibrillator implantation has generally been 2% to 3% (83–87), with the most significant complication being infection, averaging about 5% (range 1% to 20%) (83–87). Manifestations of infection may occur as long as 8.5 months after implantation and usually require explanation of the entire system (generator and leads) for successful treatment. Other complications have included myocardial infarction, pneumonia, pericardial and pleural effusions, cerebrovascular accidents, coronary artery laceration, constrictive pericarditis and, in earlier series, migration of the superior vena cava electrode (83–88).

The implantable cardioverter-defibrillator in its currently available design has several limitations in addition to complications of implantation. The device is large and requires a thoracotomy with subxiphoid or subcostal incision for lead implantation. The lack of programmability of the 30 J output requires that some patients receive shocks that have higher energy than necessary (89,90). This higher energy level may result in not only patient discomfort, but also early battery depletion. Battery life, initially very short in early devices, continues to be less than desirable, requiring reoperation to replace the generator and increasing the risk of infection. The lack of antitachycardia pacing in currently available defibrillators requires separate antitachycardia devices or, as is more commonly practiced, termination of sustained ventricular tachycardia with a high energy shock. Also, about 10% of patients undergoing defibrillator implantation need concomitant bradycardia pacing, which at present requires implantation of two devices (82,86,91,92), thereby creating the potential for inappropriate device-device interactions.

Rate programmability is a recent addition and its absence in earlier models required occasional generator changes simply to change the device rate cutoff. Current devices are committed, causing shocks to be delivered even though the arrhythmia may have terminated spontaneously during charging. In addition, the present generation defibrillator requires radiographic studies and investigation using "beep-o-grams" (93) for suspected sensing problems because the device lacks telemetry. Newer devices provide information that helps the physician determine the cause for suspected spurious shocks (Fig. 2). Cardiac arrest has been documented because of fractured defibrillator leads whose integrity could be checked only by delivery of a defibrillation pulse (86). Spurious device discharges because of failure to differentiate supraventricular from ventricular tachycardia have occurred in 10% to 40% of patients (85,87,94,95). Also, lack of telemetry makes determination of the appropriateness of a discharge difficult.

Lastly, inappropriate interactions between antiarrhythmic medications and the AICD have been described. In earlier defibrillator models, because the rate threshold for tachycardia detection was fixed, drug-induced slowing of ventricular tachycardia would occasionally reduce the ventricular tachycardia rate below the detection rate of the defibrillator and necessitate implantation of a new device. Pharmacologic therapy has also been shown to have varied effects on energy requirements for successful defibrillation, with several agents increasing this requirement (85,86). Thus, repeat electrophysiologic testing with arrhythmia induction and confirmation of successful defibrillation by the device is recommended after any change in antiarrhythmic drug therapy. Because the AICD does not have the capability for electrophysiologic testing, such testing requires transvenous catheter placement.

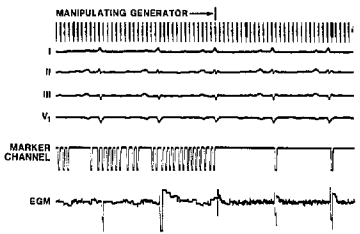

Figure 2. Determination of the cause for suspected spurious device discharges in a patient with an implanted Guardian 4203 defibrillator. Manipulation of the device generator within the pocket resulted in oversensing during sinus rhythm, as shown on the marker channel, and accounted for the occurrence of device discharges during sinus rhythm. When manipulation of the device is stopped, the device senses appropriately. Replacement of the generator solved the problem. EGM = ventricular electrogram.

New Devices

Although the perfect device is not yet available, several implantable cardioverter-defibrillators are currently undergoing clinical investigation. Many of the desirable features of the "ideal device" (Table 1) are being incorporated into these devices. Future generations will have even more.

Important features of the newer investigational devices are listed in Table 2. Although none is an ideal device, each has distinct advantages over currently available devices. Table 2 lists the devices under investigation by each of the major manufacturers. A recent review of these devices (96) has summarized the advantages and disadvantages of each. Although devices capable of antitachycardia pacing with backup defibrillation are being developed, some implantable cardioverter-defibrillators with additional features other than antitachycardia pacing (such as low energy cardioversion or bradycardia pacing, or both) may soon be approved for implantation.

Table 1. The "Ideal" Implantable Cardioverter-Defibrillator

Sensing
1. Distinguish pathologic from physiologic tachycardias
2. Differentiate two (or more) pathologic tachycardias
3. Recognize nonsustained tachycardias
4. Sensitivity programmable for different rhythms (sinus vs. ventricular tachycardia or ventricular fibrillation)

Pacing
1. Bradycardia pacing (single and dual-chamber, physiologic sensors, high output after shock)
2. Antitachycardia pacing (extrastimulus, burst or adaptive)
3. Different antitachycardia therapy for different recognized pathologic tachycardias
4. Noninvasive electrophysiologic study capabilities
5. Tachycardia prevention

Cardioversion/defibrillation
1. Low energy synchronized cardioversion
2. High energy cardioversion or defibrillation
3. Nonthoracotomy approach
4. Bidirectional, biphasic or sequential shock potential

Device features
1. Small size
2. Programmable
3. Electrograms, memory (tachycardia rate, therapy delivered, number of successful therapies)
4. Real-time clock
5. Five- to 8-year battery life
6. Automatic charging to reform capacitors

Ventak P and PRX (Cardiac Pacemakers). The Ventak P, recently approved by the Food and Drug Administration for use in the U.S., allows low energy cardioversion to 0.1 J, a useful feature for ventricular tachycardias that can be terminated with low energy shocks. Two hundred ninety two patients received the Ventak P in phase I and II trials (data on file, Cardiac Pacemakers). A total of 813 ventricular tachycardias were induced at electrophysiologic study. Sixty-one (7.5%) of the ventricular tachycardias were accelerated with a low energy shock; 56 of these 61 tachycardias had a rate >180/min. Only five "slow" (<180/min) ventricular tachycardias were accelerated with a low energy shock. Although the protocol called for ≤5 J of energy delivery, the amount of energy delivered was not a factor in determining whether ventricular tachycardia acceleration occurred.

PRX device. Phase I trials of the PRX device (Cardiac Pacemakers) have recently been completed. Like the other devices, this implantable cardioverter-defibrillator has the capability of bradycardia pacing, antitachycardia pacing, programmed stimulation and defibrillation. At the time of this writing, 47 patients have received the device (data on file, CPI). The mean patient age was 65 years and 79% of the patients had coronary artery disease. The mean ejection fraction was 33%. Monomorphic sustained ventricular tachycardia was present in 87% of the patients, polymorphic ventricular tachycardia in 2% and ventricular fibrillation in 7%. Currently, 20 of the 47 patients who have received the PRX are programmed for antitachycardia pacing. Only 16 patients have completed their 1 to 2 month follow-up visit.

Table 2. Implantable Antitachycardia Defibrillators Undergoing Clinical Investigation

	CPI PRX	Telectronics Guardian ATP 4210	Medtronic PCD 7217B	Intermedics Res-Q	Ventritex Cadence	Siemens Pacesetter Siecure
Weight (g)	220	272	197	220	240	200
Detection criteria						
Rate	+	+	+	+	+	+
Sudden onset	+	+	+	+	+	+
Tachycardia duration	+	+	+	+	+	+
Rate stability	+	–	+	+	–	+
TPM	+	–	–	–	–	–
Committed	–	–	–(VT) +(VF)	+	–	+
Defibrillation detection zone (no.)	1	1	1	1	1	1
Tachycardias differentiated (no.)	2	2	1	4	2	2
Bradycardia pacing	+	+	+	+	+	+
Antitachycardia pacing	+	-	+	+	+	+
Programmable	+	-	+	+	+	+
Maximal shock energy (J)	34	40	34	40	34	40
Minimal cardioversion energy (J)	0.1	0.5	0.2	0.1	0.1	2.5
Synchronized shocks	+	+	+	+	+	+
Defibrillator patches (no.)	2	2	2 or 3	2	2	2
Sequential shocks or bidirectional shocks	–	–	+	–	–	–
Biphasic shocks	–	–	–	+	+	–
Real-time electrogram	-	+	-	+	+	+
Noninvasive EPS	-	VVT	+	+	+	+

EPS = electrophysiologic study; TPM = turning point morphology (a modified form of the probability density function); VF = ventricular fibrillation; VT = ventricular tachycardia; VVT = triggered ventricular pacing; – = absent; + = present.

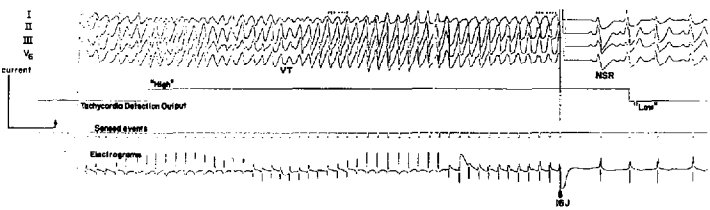

Figure 3. Testing of defibrillation threshold. Rapid, polymorphic ventricular tachycardia is induced with alternating current and is terminated with a shock of 16 J delivered by the Implant Support Device in a patient receiving an implanted Telectronics Guardian 4203 defibrillator. It is evident that intracardiac electrograms are adequately sensed during ventricular tachycardia. The "tachycardia detection output" is a logic signal generated by the Guardian circuitry when the tachycardia detection criteria are being fulfilled. The tachycardia detection output is represented as "high" when tachycardia has been detected and "low" when no tachycardia is present. NSR = normal sinus rhythm; VT = ventricular tachycardia.

Nine patients have received spontaneous shocks and no tachyarrhythmic deaths have been reported.

Guardian 4202/3 and ATP (4210) (Telectronics). The Guardian defibrillator also has low energy synchronous cardioversion, but its predominant advantages are: 1) bradycardia pacing, and 2) reconfirmation that ventricular tachycardia is still present and the ability to "dump" the charge internally if the arrhythmia has terminated before delivery of the shock (Table 2). Our preliminary report (97) of 24 patients with an implanted Guardian 4202/3 defibrillator showed that seven patients had had episodes of diverted shocks (that is, the capacitors charged but no shock was delivered) for nonsustained ventricular tachycardia. Reprogramming the device decreased the frequency of or eliminated these diverted shocks in four patients and no patient had an inappropriate shock. One patient who had received frequent spurious shocks (shocks not for ventricular tachycardia) from an automatic implantable cardioverter-defibrillator had no spurious shocks for 7 months after the device was replaced with a Guardian defibrillator. Thus, multiprogrammability, telemetry, permanent ventricular demand (VVI) pacing, tachycardia reconfirmation and a programmable detection algorithm offered improvements over first generation devices. Figure 3 shows intraoperative testing with the Guardian defibrillator device.

The Telectronics Guardian ATP (model 4210) is also currently under investigation. This device has bradycardia pacing (low and high output), antitachycardia pacing, a maximal shock energy of 40 J and a minimal shock energy of 0.5 J. Its shocks are synchronized and are delivered over two defibrillator patches. The device is not capable of noninvasive programmed stimulation at this time, but programmed stimulation can be performed using ventricular triggered (VVT) pacing techniques through the device. It has extensive telemetry capabilities.

There are very preliminary implant data on the Guardian ATP device. In one series (98), five patients received this system. Two of the five patients had several spontaneous ventricular tachycardia episodes that were terminated successfully by antitachycardia pacing or defibrillation, or spontaneous ventricular fibrillation episodes that were successfully defibrillated over a 2 month follow-up period. All five patients required bradycardia support.

PCD (Medtronic). The Medtronic PCD weighs 197 g in its current design (7217B). It is a committed device for ventricular fibrillation but not for ventricular tachycardia. It has bradycardia pacing capabilities, is programmable and has a maximal shock energy of 34 J and a minimal cardioversion energy of 0.2 J. Shocks can be delivered over two or three patches and bidirectional/sequential shocks may be delivered through the device. It cannot deliver biphasic shocks. A nonthoracotomy lead system using either a coronary sinus lead or subcutaneous patch in the left thorax may be utilized. It can perform noninvasive electrophysiologic testing (Table 2).

A report by Yee et al. (99) revealed preliminary results in four patients with the PCD 7215. Over a follow-up period of 1.5 to 23 months, 161 spontaneous episodes of ventricular tachycardia and 9 episodes meeting the ventricular fibrillation criterion were detected and treated by the device. Ramp pacing terminated 140 ventricular tachycardia episodes and was successful 88.5% of the time, whereas 10 episodes (7.2%) required low energy epicardial cardioversion (4 to 10 J). Six episodes (4.3%) terminated spontaneously before delivery of therapy. All nine spontaneous episodes of ventricular fibrillation were defibrillated with shocks of 10 to 15 J. No complications, malfunction of the device or inappropriate delivery of therapy was observed.

We have reported (100) our experience with the PCD (Medtronic 7216) in 12 patients. Shock therapy was administered over two epicardial patches in five patients and over three patches in six patients (in a sequential or simultaneous

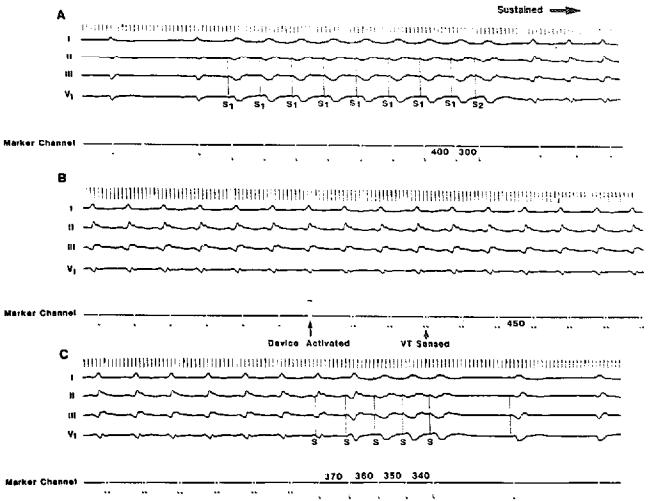

Figure 4. Noninvasive testing of the Medtronic PCD device in a patient with sustained ventricular tachycardia. In **panel A**, sustained ventricular tachycardia is induced with a single ventricular extrastimulus (S2) after a pacing drive train (S1) using a programmer and the implanted device. In **panel B**, sustained ventricular tachycardia having a cycle length of 450 ms is detected by the device after it is activated. In **panel C**, the arrhythmia has fulfilled the criteria for ventricular tachycardia detection. A ramp pacing run (previously programmed into the device to deliver five impulses on the first run, decrementing by 10 ms per impulse) successfully terminates ventricular tachycardia. A paced (fusion) complex follows before resumption of sinus rhythm. Abbreviation as in Figure 3.

fashion), or through transvenous leads and a subcutaneous patch (one patient). Nine patients had automatic therapy for spontaneous arrhythmias: pacing for ventricular tachycardia in seven, shocks for ventricular tachycardia in four and shocks for ventricular fibrillation in three. Four patients were unaware of ventricular tachycardia onset or termination. Failure to detect and terminate ventricular tachycardia that was slower than the detection rate was corrected by reprogramming (two patients). One patient had pacing-induced acceleration of ventricular tachycardia to ventricular fibrillation with subsequent detection and automatic defibrillation. One patient with slow ventricular tachycardia (120/min) had sinus tachycardia that triggered ventricular tachycardia pacing that, in turn, induced ventricular tachycardia and subsequent shocks. Neither mechanical device failure nor failure to recognize a tachycardia occurred. Figure 4 illustrates some of the features of this device, namely, noninvasive programmed stimulation, antitachycardia pacing and bradycardia pacing.

An experience with 10 patients with an implanted PCD defibrillator is now in press (101). The patients received model 7216A or 7217B. All patients had coronary disease and sustained ventricular tachycardia not suppressed by antiarrhythmic drug therapy; two patients had a nonthoracotomy lead system. The lowest effective defibrillation energy ranged from 5 to 18 J (mean 12.2) for the epicardial electrode systems and was 15 and 18 J for the nonthoracotomy lead implants. Follow-up ranged from 7 to 19 months (mean 13.8). Spontaneous tachyarrhythmia episodes were detected and treated by the device in six patients; five of them received "staged" (tiered) therapy. No deaths occurred and no hospital admissions were necessary for device or ventricular tachyarrhythmia-related complications.

To date, 347 patients in the U.S. have received the PCD defibrillator (models 7216A/7217B) (data on file, Medtronic). The mean follow-up time is 6 months, with a maximal follow-up time of 18.6 months. The mean patient age was 58 years. Indications for implantation were ventricular fibrilla-

tion (28%), ventricular tachycardia (52%) and ventricular tachycardia/fibrillation (19%). Seventy-four percent of patients had coronary artery disease; the mean ejection fraction was 34%. The mean defibrillation threshold was 9 J. Four thousand twenty-nine episodes of spontaneous ventricular tachycardia have occurred during follow-up and the success rate for automatic termination of ventricular tachycardia by the device was 97.1%. The actuarial survival rate (for sudden cardiac death) was 97.2%.

Cadence (Ventritex). This 240 g device has the capability of performing antitachycardia pacing, bradycardia pacing and defibrillation with a maximal energy of 34 J. Synchronized cardioversion to 0.1 J may be utilized. The shocks are delivered over two patches. This device can deliver a shock with use of a biphasic energy waveform. Noninvasive electrophysiologic testing can be performed with the Cadence (Table 2) and ventricular electrograms can be recorded with it and possibly aid in the diagnosis of spontaneous arrhythmias in patients with the device.

Winkle et al. (102) have described their experience with the Cadence in 58 consecutive patients. A total of 350 episodes of ventricular tachyarrhythmia, including 68 episodes of sustained ventricular tachycardia and 282 episodes of ventricular fibrillation, were induced. Antitachycardia pacing was attempted in 45 of the 68 episodes of ventricular tachycardia. It was successful in 23 episodes, failed in 9 and accelerated the tachycardia in 13. In all 22 cases of failure or acceleration the arrhythmia was terminated by cardioversion or delivery of ventricular fibrillation therapy. An attempt was made to convert 23 episodes of ventricular tachycardia with shocks delivered at an average energy level of 6 J. Sixteen episodes were successfully terminated by the shock; during 6 episodes the arrhythmia stopped during charging and the shock was not delivered to the patient. In one episode ventricular tachycardia was accelerated to ventricular fibrillation that was subsequently successfully terminated by the device. The device terminated a total of 303 episodes of ventricular fibrillation in 172 cases by the first shock delivered (average energy level 10 J). Forty episodes of ventricular fibrillation terminated spontaneously during the initial charging and no shock was delivered. The first shock failed in 91 instances and a second shock averaging 25 J was required. It was successful in 70 instances and unsuccessful in 6; in the remaining 15 instances, the arrhythmia terminated during second-shock charging and no shock was delivered. All six arrhythmias in which a second shock failed were terminated successfully by a third shock at an energy level averaging 38 J. Thus, all 350 episodes of induced arrhythmias either terminated spontaneously or were successfully terminated by the device. Bradycardia pacing, noninvasive programmed stimulation and stored diagnostic data functioned without detectable problems.

A recent report (103) described the value of ventricular electrograms in the diagnosis of arrhythmias causing electrical devices to administer shock therapy. Three patients had the Cadence defibrillator system implanted. By analyzing the electrogram rate and RR interval stability and configuration, a definitive cause for device activation was established in all three patients (atrial fibrillation, polymorphic ventricular tachycardia and rate-sensing lead disruption, respectively).

Res-Q (Intermedics). This is a defibrillator that also has the capability of antitachycardia pacing and bradycardia pacing. Contoured patches have been developed to be compatible with the device. These patches, along with biphasic shocks, may reduce defibrillation threshold in some patients. The Res-Q can be used for noninvasive electrophysiologic testing (Table 2).

A preliminary experience with the Res-Q was reported by Nathan et al. (104) in three patients. All units were implanted with large surface area asymmetrical contoured patches placed epicardially. Defibrillation thresholds were 0.8, 5.2, and 3.2 J, respectively, in the three patients. At testing after implantation, all devices terminated ventricular tachycardia with pacing and ventricular fibrillation with defibrillation. At follow-up (18, 14 and 7 weeks after implantation, respectively), one device appropriately treated spontaneous ventricular fibrillation and two devices appropriately paced for ventricular tachycardia. Two of the patients were regularly using bradycardia pacing, and all patients were receiving antiarrhythmic medications to reduce the frequency of arrhythmias. There were no major problems.

Siecure (Siemens/Pacesetter). This is a 200 g defibrillator with antitachycardia and bradycardia pacing. It is a committed device in its current design and can deliver a maximal shock of 40 J and a minimal cardioversion energy of 2.5 J. The shocks are delivered over two patches. It does not have sequential shock, bidirectional shock or biphasic shock capabilities. Noninvasive electrophysiologic testing can be performed from the device (Table 2).

At the present time, five patients have received the Siecure device (Siemens/Pacesetter) in England. Of these five patients, none has yet had a spontaneous arrhythmia. Both epicardial and endocardial pacing electrodes have been used. The shock electrodes were all epicardial (data on file, Siemens/Pacesetter).

Future Directions

Nonthoracotomy lead systems. Although much work has explored the applicability of transvenous cardioversion and defibrillation (105–108), more recently a nonthoracotomy system using one or more transvenous catheters and a chest wall electrode for defibrillation (Fig. 5) has been tested clinically (109,110). Combinations of electrodes in the superior vena cava, coronary sinus and right ventricular apex are being tested together with the chest wall electrode. In general, defibrillation thresholds of ≤18 J can be achieved in about 75% of patients using nonthoracotomy lead placement often employing sequential shocks. It would seem likely that improvements in electrode design and energy waveform will increase that figure to 80% to 90% and will make this the method of choice for cardioverter/defibrillator implantation.

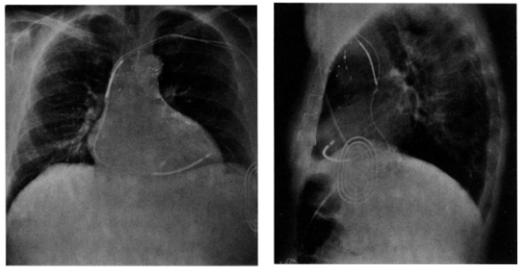

Figure 5. Posteroanterior (**left panel**) and *lateral (right panel) chest radiographs of* a patient who received a nonthoracotomy lead system. The patient has a Medtronic 7216A defibrillator. Transvenous leads are in the right ventricle and right atrium. Sensing is accomplished from the right ventricle. Defibrillation occurs through two sequential pathways using three defibrillating leads: right ventricle, superior vena cava-right atrial junction and submuscular patch (**seen over the left hemithorax**). One of these leads serves as a "common" electrode.

Energy wave forms. Bidirectional square wave or truncated exponential shocks provide successful defibrillation more than monophasic shocks in experimental and clinical studies (111,112). Use of a biphasic waveform should require lower energy shocks that will result in potentially less patient discomfort, less battery depletion and possibly a higher percentage of acceptable defibrillation thresholds using nonthoracotomy lead systems (113).

Sequential pulse defibrillation. Whether sequential pulse defibrillation offers any advantage over single pulse defibrillation is controversial. Studies in pigs (114) and in humans (115) suggest a reduction in defibrillation threshold using sequential, as compared with single, shocks. However, other studies (116) have shown a comparable defibrillation threshold with both techniques. It may be that sequential shocks offer an advantage when defibrillation threshold elevated. It does seem important, however, that the defibrillating energy pass through the intraventricular septum because all pathways incorporating the septum have a lower defibrillation threshold than those that do not (117).

Conclusions. Major advances have been, and continue to be, made in the field of antitachycardia devices. As we approach the development of the ideal device that can be implanted without thoracotomy, the therapeutic choices of physicians who care for patients with life-threatening ventricular arrhythmias continue to increase. The six devices currently under development that are capable of tiered therapy represent a major advance in the management of patients with life-threatening ventricular arrhythmias.

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